

**REMARKS**

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

**I. CLAIM STATUS & AMENDMENTS**

Claims 1-9 were pending in this application when last examined and stand rejected.

Claims 1 and 5 have been amended.

Claim 4 has been cancelled without prejudice or disclaimer thereto. Applicants reserve the right to file a continuation or divisional application on any canceled subject matter.

Claims 1-3 and 5-9 are now pending in this application.

Support for the amendments to claims 1 and 5 can be found in original claim 4 and in the specification at page 8, lines 11-29.

Therefore, no new matter has been added by this amendment.

**II. FOREIGN PRIORITY DATE**

Acknowledgment has been made of the claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f) to Japanese Application 11/268745. However, in item 12(c)1 on page 1 and in paragraph 1 on page 2 of Office Action it is indicated that a certified copy and translation of the foreign priority document have not been received.

Attached herewith is a copy of Form PCT/IB/304 indicating that a certified copy of the priority document was forwarded to WIPO during prosecution of the international application. Consequently, a copy should have been forwarded to the PTO from the International Bureau. Applicants respectfully request that the file be checked again for a copy of the certified priority document. If necessary, a copy of the certified priority document will be submitted in due course.

**III. REJECTION UNDER 35 U.S.C. § 102**

Claims 1-9 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Livak et al., U.S. Patent No. 5,723,591. See Office Action, item 1 on pages 2-3.

This rejection is respectfully traversed as applied to the amended claims in view of the following remarks.

Livak fails to disclose or suggest each and every element of the claimed invention, namely a probe comprising an intercalator or an energy-absorbing substance that specifically binds a double-stranded nucleic acid due to the hybridization of the probe with a target nucleic acid whereby the energy transfer from the labeling substance to the energy-absorbing substance is intercepted resulting in no quenching.

The claimed invention relates to a probe comprising a nucleic acid carrying a labeling substance that release energy and an energy-absorbing substance, such as an intercalator, that is capable of absorbing the energy released from the labeling substance. As discussed in the specification on page 5, lines 3-9, the energy transfer from the labeling substance to the energy-absorbing substance or intercalator is intercepted by the hybridization of the probe with a target nucleic acid. This, in turn, releases the light from the labeling substance.

This is further discussed in the specification at page 8, lines 11-29. When the probe that is completely complementary to the target nucleic acid hybridizes with a sample, the intercalator or the energy-absorbing substance on the probe specifically binds the double-stranded nucleic acid. This prevents the quenching of the labeling substance. See also Figure 1 in the specification. On the other hand, when the probe does not hybridize with a sample, the intercalator or the energy-absorbing substance on the probe does not interact with the double-stranded nucleic acid which in turn results in quenching of the labeling substance. Thus, upon hybridization with the nucleic acid sample, the presence of light released from the labeling substance indicates that the probe and the target nucleic acid are hybridized.

Livak discloses an oligonucleotide probe carrying a reporter molecule and a quencher molecule, wherein the fluorescence of the reporter molecule is unquenched when a target oligonucleotide is hybridized to the probe.

Livak neither discloses nor suggests that a quencher molecule binds to or intercalates to a double-stranded nucleic acid or that the fluorescence of the reporter molecule is thereby unquenched. As seen in Figure 2 in Livak (and as discussed in column 7, lines 10-25) the fluorescence of the reporter molecule is unquenched when a target molecule is hybridized to the

probe and a hairpin structure of the probe is thereby straightened. In other words, when the probe is hybridized to the target sequence, the probe of Livak undergoes a conformational change whereby the quencher is not positioned close enough to the reporter molecule to quench the fluorescence. See column 7, lines 15-20.

By contrast, the mechanism of the probe of amended claim 1 does not involve such conformational change. Instead, the claimed probe is characterized in that the energy-absorbing substance, such as an intercalator, specifically binds the double-stranded nucleic acid due to the hybridization of the probe with a target nucleic acid. This causes the energy transfer from the labeling substance to the energy-absorbing substance to be intercepted which results in no quenching. The claimed invention is distinguishable from Livak, because Livak fails to disclose or suggest this interaction.

In view of the above, the rejection of claims 1-9 under 35 U.S.C. §102(b) is untenable and should be withdrawn.

**CONCLUSION**

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is now in condition for allowance and early notice to that effect is hereby requested.

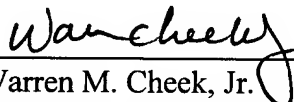
If it is determined that the application is not in condition for allowance, the Examiner is invited to telephone the undersigned attorney at the number below if he or she has any suggestions to expedite allowance of the present application.

Respectfully submitted,

Akio YAMANE

THE COMMISSIONER IS AUTHORIZED  
TO CHARGE ANY DEFICIENCY IN THE  
FEES FOR THIS PAPER TO DEPOSIT  
ACCOUNT NO. 23-0975

By: \_\_\_\_\_

  
Warren M. Cheek, Jr.  
Registration No. 33,367  
Attorney for Applicants

WMC/JFW/kes  
Washington, D.C. 20006-1021  
Telephone (202) 721-8200  
Facsimile (202) 721-8250

June 30, 2004

Attorney Docket No.: 2002\_0401A  
Serial No.: 10/088,598  
June 30, 2004

**ATTACHMENT TO AMENDMENT AND REPLY:**

1. Form PCT/IB/304

## PATENT COOPERATION TREATY

PCT

NOTIFICATION CONCERNING  
SUBMISSION OR TRANSMITTAL  
OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

From the INTERNATIONAL BUREAU

To:

SATO, Kazuo  
Kyowa Patent & Law Office  
Room 323, Fuji Bldg.  
2-3, Marunouchi 3-chome  
Chiyoda-ku, Tokyo 100-0005  
JAPON

KYOWA  
PATENT &

REC - 4. 2000

RECEIVED

Date of mailing (day/month/year) 20 November 2000 (20.11.00)	<b>IMPORTANT NOTIFICATION</b>
Applicant's or agent's file reference 127533-654	
International application No. PCT/JP00/06524	
International publication date (day/month/year) Not yet published	
Applicant WAKUNAGA PHARMACEUTICAL CO., LTD. et al	International filing date (day/month/year) 22 September 2000 (22.09.00)  Priority date (day/month/year) 22 September 1999 (22.09.99)

- The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
- An asterisk(\*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

<u>Priority date</u>	<u>Priority application No.</u>	<u>Country or regional Office or PCT receiving Office</u>	<u>Date of receipt of priority document</u>
22 Sept 1999 (22.09.99)	11/268745	JP	15 Nove 2000 (15.11.00)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No. (41-22) 740.14.35	Authorized officer  Somsak Thiphrakesone  Telephone No. (41-22) 338.83.38
--	---

Form PCT/IB/304 (July 1998)

003669409